



Cell 4.17 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Raju Kucherlapati et al.
Application No. : 10/658,521 Confirmation No.: Not yet assigned
Filed : September 8, 2003
For : HUMAN ANTIBODIES DERIVED FROM IMMUNIZED
XENOMICE
Group Art Unit : Not yet assigned
Examiner : Not yet assigned

New York, New York
November 24, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

TRANSMITTAL LETTER FOR
INFORMATION DISCLOSURE STATEMENT

Sir:

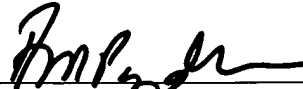
Transmitted herewith is an Information Disclosure Statement in the above-identified application. This Statement is submitted:

- ☒ within three months of the application filing date;
☐ more than three months from the application filing date but before the mailing date of the first Office Action on the merits.

In accordance with 37 C.F.R. § 1.97, submission of this Statement requires no fee. However, if for any reason a fee is due, the Director is hereby authorized to

charge payment of any fees required in connection with this Information Disclosure
Statement to Deposit Account No. 06-1075.

Respectfully submitted,

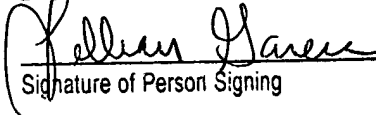


Jane T. Gunnison (Reg. No. 38,479)
Attorney for Applicants
R. Minako Pazdera (Reg. No. 46,984)
Agent for Applicants
c/o FISH & NEAVE
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax.: (212) 596-9090

I hereby certify that this
Correspondence is being
deposited with the U.S.
Postal Service as First
Class Mail in an envelope
Addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450 on

November 24, 2003

Lillian Garcia


Signature of Person Signing



CELL 4.17 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : R. Kucherlapati et al.
Application No. : 10/658,521 Confirmation No.: Not yet assigned
Filed : September 8, 2003
For : HUMAN ANTIBODIES DERIVED FROM IMMUNIZED
XENOMICE
Group Art Unit : Not yet assigned
Examiner : Not yet assigned

New York, New York
November 24, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants, through their attorney and agent, make of record the following documents.¹

<u>Applicant</u>	<u>U.S. Patents</u> <u>Patent No.</u>	<u>Issue Date</u>
Bertling et al.	4,950,599	August 21, 1990
Taketo et al.	4,959,313	September 25, 1990
Fell et al.	5,204,244	April 20, 1993
Handley et al.	5,286,647	February 15, 1994
Lonberg et al.	5,545,806	August 13, 1996

¹ A completed Form PTO-1449 listing these documents, is attached hereto.

U.S. Patents

<u>Applicant</u>	<u>Patent No.</u>	<u>Issue Date</u>
Surani et al.	5,545,807	August 13, 1996
Lonberg al.	5,569,825	October 29, 1996

FOREIGN PATENT DOCUMENTS

<u>Publication Number</u>	<u>Publication date</u>
WO 90/04036	April 19, 1990
WO 91/00906	January 24, 1991
WO 91/10741	July 25, 1991
WO 92/03918	March 19, 1992
WO 92/22645	December 23, 1992
WO 93/05165	March 18, 1993
WO 93/12227	June 24, 1993
WO 94/00569	January 6, 1994
WO 94/02602	February 3, 1994
WO 94/25585	November 10, 1994
WO 96/34096	October 31, 1996
EP 0 298 807 A1	January 11, 1989
EP 0 315 062 B1	May 10, 1989
EP 0 322 240 B1	June 28, 1989
EP 0 459 372 A3	December 4, 1991
EP 0 463 151 B1	January 2, 1992

Other References

Albertson, et al., "Construction and characterization of a yeast artificial chromosome library containing seven haploid human genome equivalents," *Proc. Natl. Acad. Sci.* 87:4256-4260 (1990)

Aldhous, "Transgenic mice display a class (switching) act," *Science* 262:1212

- Ayares, et al., "Sequence homology requirements for intermolecular recombination in mammalian cells," *Proc. Natl. Acad. Sci.* 83:5199-5203 (1986)
- Berman, et al., "Content and organization of the human Ig V_H locus: definition of three new V_H families and linkage to the Ig C_H locus" *EMBO J.* 7:727-738 (1988)
- Blankenstein, et al., "Immunoglobulin V_H region genes of the mouse are organized in overlapping clusters" *Eur. J. Immunol.* 17:1351-1357 (1987)
- Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice," *Proc. Natl. Acad. Sci.* 85:836-840 (1988)
- Brownstein, et al., "Isolation of single-copy human genes from a library of yeast artificial chromosomes", *Science* 244:1348-1351 (1989)
- Bruggemann, et al., "A repertoire of monoclonal antibodies with human heavy chains from transgenic mice," *Proc. Natl. Acad. Sci.* 86:6709-6713 (1989)
- Bruggemann, et al., "Construction, function and immunogenicity of recombinant monoclonal antibodies," *Behring Inst. Mitt.* 87:21-24 (1990)
- Bruggemann, et al., "Human antibody production in transgenic mice: expression from 100 kb of the human IgH locus," *Eur. J. Immunol.* 21:1323
- Bruggemann, et al., "Strategies for expressing human antibody repertoires in transgenic mice," *Immunology Today* 17:391-397 (1996)
- Burke, et al., "Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors," *Science* 236:806-812 (1987)
- Buttin, et al., "Exogenous Ig rearrangement in transgenic mice: a new strategy for human monoclonal antibody production," *Trends in Genetics* 3(8):205-206 (1987)
- Cai, J. et al., "Extensive and selective mutation of a rearranged V_H5 gene in human B cell chronic lymphocytic leukemia," *J. Exp. Med.*, 176, 1073-1081 (1992)
- Capecchi, M.R., "Altering the genome by homologous recombination," *Science* 244:1288-92 (1989)
- Chen et al., "Immunoglobulin gene rearrangement in B cell deficient mice generated by targeted deletion of the J_H locus," *International Immunology* 5:647-656 (1993)
- Choi, et al., "RNA splicing generates a variant light chain from an aberrantly rearranged K gene," *Nature* 286:776-779 (1980)
- Choi, et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome," *Nature Genetics* 4:117-123 (1993)
- Cook, G.P. et al., I.M., "The human immunoglobulin V_H repertoire," *Immunology Today* 16:237-242 (1995)
- Corvalon, et al., "Generation of fully human high affinity monoclonal antibodies to EGF receptor in mice," *Journal of Allergy and Clinical Immunology* 99:S214 (1997)
- Cox, et al., "A directory of human germ-line V_X segments reveals a strong bias in their usage," *Eur. J. Immunol.* 24:827-836 (1994)

- Davies, et al., "Targeted alterations in yeast artificial chromosomes for inter-species gene transfer," *Nucleic Acids Res.* 20:2693-2698 (1992)
- Doetschman, et al., "Targeted mutation of the Hprt gene in mouse embryonic stem cells," *Proc. Natl. Acad. Sci.* 85:8583-8587 (1988)
- Dorfman, N.A. "The optimal technological approach to the development of human hybridomas," *Journal of Biological Response Modifiers* 4:213-239 (1986)
- Eliceiri, et al., "Stable integration and expression in mouse cells of yeast artificial chromosomes harboring human genes," *Proc. Natl. Acad. Sci.* 88:2179-2183 (1991)
- Ellison, et al., "The nucleotide sequence of a human immunoglobulin C γ 1 gene," *Nucleic Acids Research*, 10:4071-4079 (1982)
- Emery, S.C. and Adair, J.R., "Humanised monoclonal antibodies for therapeutic applications," *Expert Opinion on Investigation Drugs*, 3:241-251 (1994)
- Fishwild, et al., "High-avidity human IgG κ monoclonal antibodies from a novel strain of minilocus transgenic mice," *Nature Biotech.*, 14:845-851 (1996)
- Garza, et al., "Mapping the *drosophila* genome with yeast artificial chromosomes", *Science* 246:641-646 (1989)
- Gnirke, et al., "Cloning and *in vivo* expression of the human GART gene using yeast artificial chromosomes", *EMBO J.* 10(7):1629-1634 (1991)
- Green, L.L. et al., "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACs," *Nat Genet.* 7:13-21 (1994)
- Huber, et al., "The human immunoglobulin κ locus. Characterization of the partially duplicated L regions," *Eur. J. Immunol.* 23:2860-2967 (1993)
- Huxley, et al., "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion," *Genomics* 9:742-750 (1991)
- Ikematsu, et al., "Clonal analysis of a human antibody response. II. sequences of the V_H genes of human IgM, IgG, IgA to rabies virus reveal preferential utilization of V_HIII segments and somatic hypermutation," *The Journal of Immunology*, 150:1325-1337 (1993).
- Jakobovits, et al., "Analysis of homozygous mutant chimeric mice: Deletion of the immunoglobulin heavy-chain joining region blocks B-cell development and antibody production," *Proc. Natl. Acad. Sci.* 90:2551-2555 (1993)
- Jakobovits, et al., "Germ-line transmission and expression of a human-derived yeast artificial chromosome," *Nature* 362:255-258 (1993)
- Jakobovits, "Humanizing the mouse genome," *Current Biology* 4:761-763 (1994)
- Jakobovits, et al. "Production of antigen-specific human antibodies from mice engineered with human heavy and light chain YACs," *Annals of the New York Academy of Sciences* 764:525-535 (1995)
- Jakobovits, A., "Production of fully human antibodies by transgenic mice," *Current Opinion in Biotechnology* 6:561-566 (1995)

- Jakobovits et al., "Humoral immunity in mice engineered with megabase human heavy and kappa light chain YACs," *Journal of Allergy and Clinical Immunology* 99:S113 (1997)
- Johnson et al., "Targeting of nonexpressed genes in embryonic stem cells via homologous recombination," *Science* 245:1234-1236 (1989)
- Joyner, et al., "Production of a mutation in mouse En-2 gene by homologous recombination in embryonic stem cells," *Nature* 338:153-155 (1989)
- Koller, et al., "Inactivating the β 2-microglobulin locus in mouse embryonic stem cells by homologous recombination" *Proc. Natl. Acad. Sci.* 86:8932-8935 (1989)
- Kucherlapati, R., "Homologous recombination in mammalian somatic cells," *Prog. Nucleic Acid Res. Mol. Biol.* 36:301-310 (1989)
- Li Y. et al., "The binding specificity of human V_H4-34 (V_H4-21) encoded antibodies is determined by both V_H framework region 1 and complementarity determining region 3," *J. Mol. Biol.* 256:577-589 (1996)
- Lonberg et al., "Antigen-specific human antibodies from mice comprising four distinct genetic modifications," *Nature* 368:856-859 (1994)
- Lonberg, et al., "Human antibodies from transgenic mice," *International Reviews of Immunology*, 13:65-93 (1995).
- Mansour et al., "Disruption of the proto-oncogene int-2 in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes," *Nature* 336:348-352 (1988)
- Matsuda, et al., "Structure and physical map of 64 variable segments in the 3' 0.8- megabase region of the human immunoglobulin heavy chain locus," *Nature Genetics* 3:88-94 (1993)
- Max, et al., "Sequences of five potential recombination sites encoded close to an immunoglobulin k constant region gene," *Proc. Natl. Acad. Sci.* 76(7):3450-3454 (1979)
- Mendez, et al., "Analysis of the structural integrity of YACs comprising human immunoglobulin genes in yeast and in embryonic stem cells," *Genomics*, 26:294-307 (1995)
- Mendez, et al., "Functional transplant of megabase human immunoglobulin loci recapitulates human antibody response in mice," *Nature Genetics*, 15:146-156 (1997)
- Miller, et al., "Structural alterations in J regions of mouse immunoglobulin λ genes are associated with differential gene expression," *Nature* 295:428-430 (1982)
- Morrison, S. "Success is in the specification," *Nature*, 369:812-813 (1994)
- Mortensen, et al., "Production of homozygous mutant ES cells with a single targeting construct," *Mol. Cell. Biol.* 12(5):2391-2395 (1991)
- Orkin, et al., "Mutation in an intervening sequence splice junction in man," *Proc. Natl. Acad. Sci.* 78(8):5041-5045 (1981)
- Pachnis, et al., "Transfer of a yeast artificial chromosome carrying human DNA from *Saccharomyces cerevisiae* into mammalian cells," *Proc. Natl. Acad. Sci.* 87:5109-5113 (1990)
- Pavan, et al., "Modification and transfer into an embryonal carcinoma cell line of a 360-kilobase human-derived yeast artificial chromosome," *Mol. Cell. Biol.* 10(8):4163-4169 (1990)

Rajewsky, et al., "Evolutionary and somatic selection of the antibody repertoire in the mouse," *Science* 238:1088-1094 (1987)

Ramirez-Solis, et al., "Chromosome engineering in mice," *Nature* 378:720-724 (1995)

Sakano, et al., "Sequences at the somatic recombination sites of immunoglobulin light-chain genes," *Nature* 280:288-294 (1979)

Sakano, et al., "Two types of somatic recombination are necessary for the generation of complete immunoglobulin heavy-chain genes," *Nature* 286:676-683 (1980)

Sakano, et al., "Identification and nucleotide sequence of a diversity DNA segment (D) of immunoglobulin heavy chain genes," *Nature* 290:562-565 (1981)

Sanz, I., "Multiple mechanisms participate in the generation of diversity of human H chain CDR3 regions," *J. of Immunol.* 147:1720-1729 (1991)

Schedl, et al., "Transgenic mice generated by pronuclear injection of a yeast artificial chromosome," *Nucleic Acids Research*, 20:3073-3077 (1992)

Schedl, et al., "A method for the generation of YAC transgenic mice by pronuclear microinjection," *Nucleic Acids Research* 21(20):4783-4787 (1993)

Schedl, et al., "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice," *Nature* 362:258-261 (1993)

Schwartzberg, et al., "Germ-line transmission of a c-abl mutation produced by targeted gene disruption in ES cells," *Science*, 246:799-803 (1989)

Seidman, et al., "A Mutant immunoglobulin light chain is formed by aberrant DNA- and RNA-splicing events," *Nature* 286:779-783 (1980)

Shimizu, et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse," *Proc. Natl. Acad. Sci.* 86:8020-8023 (1989)

Shin, et al., "Physical map of the 3' region of the human immunoglobulin heavy chain locus: clustering of autoantibody-related variable segments in one haplotype," *EMBO J.* 10:3641-3645 (1991)

Strauss, et al., "Germ line transmission of a yeast artificial chromosome spanning the murine α_1 (1) collagen locus," *Science* 259:1904-1907 (1993)

Taggart, et al., "Stable antibody-producing murine hybridomas," *Science* 219:1228-1230 (1983)

Takahashi, et al., "Structure of human immunoglobulin gamma genes: implications for evolution of a gene family," *Cell* 29:671-679 (1982)

Taki, et al., "Targeted insertion of a variable region gene into the immunoglobulin heavy chain locus," *Science* 262:1268-1271 (1993)

Taylor, et al., "Human immunoglobulin transgenes undergo rearrangement, somatic mutation and class switching in mice that lack endogenous IgM," *International Immunol.* 6:579-591 (1994)

Taylor, et al., "A transgenic mouse that expresses a diversity of human sequence heavy and light chain immunoglobulins," *Nucleic Acids Research* 20:6287-6295 (1992)

Thomas, et al., "Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells," *Cell* 51: 503-512 (1987)

Traver, et al., "Rapid screening of a human genomic library in yeast artificial chromosomes for single-copy sequences," *Proc. Natl. Acad. Sci.* 86:5898-5902 (1989)

Treisman, et al., "Specific transcription and RNA splicing defects in five cloned β -thalassaemia genes," *Nature* 302:591-596 (1983)

Tuaillon, et al., "Analysis of direct and inverted DJ_H rearrangements in a human Ig heavy chain transgenic minilocus," *J. Immunol.* 154:6453-6465 (1995)

Tuaillon, et al., "Human immunoglobulin heavy-chain minilocus recombination in transgenic mice: gene-segment use in μ and γ transcripts," *Proc. Natl. Acad. Sci. U.S.A.*, 90:3720-3724 (1993)

Tucker, et al., "Mouse IgA heavy chain gene sequence: implications for evolution of immunoglobulin hinge exons," *Proc. Natl. Acad. Sci.* 78:7684-7688 (1981)

Wagner, et al., "The diversity of antigen-specific monoclonal antibodies from transgenic mice bearing human immunoglobulin gene miniloci," *Eur. J. Immunol.* 24:2672-2681 (1994)

Weichhold, et al., "The human immunoglobulin κ locus consists of two copies that are organized in opposite polarity," *Genomics* 16:503-511 (1993)

Winter, et al., "Making antibodies by phage display technology," *Annual Review of Immunology*, 12:433-455 (1994).

Yamada, M., et al., "Preferential utilization of specific immunoglobulin heavy chain diversity and joining segments in adult human peripheral blood B lymphocytes," *J. Exp. Med.* 173:395-407 (1991)

Yamamura, et al., "Cell-type specific and regulated expression of a human γ heavy-chain immunoglobulin gene in transgenic mice", *Proc. Natl. Acad. Sci.* 83:2152-2156 (1986)

Yancopoulos, et al., "Reconstruction of an immune system," *Science* 241:1581-1583 (1988)

Yancopoulos, et al., "Developmentally controlled and tissue-specific expression of unrearranged V_H gene segments," *Cell* 40:271-281 (1985)

Yang, et al., "Human monoclonal antibodies to human TNF-alpha generated from mice carrying human Ig loci," *Journal of Allergy and Clinical Immunology* 99:S15 (1997)

Zachau, "The human immunoglobulin κ locus and some of its acrobatics," *J. Biol. Chem.* 371:1-6 (1990)


Zijlstra, et al., "Germ-line transmission of a disrupted β 2-microglobulin gene produced by homologous recombination in embryonic stem cells," *Nature* 342:435-438 (1989)

Copies of all the documents listed above were submitted by applicants in parent U.S. Patent Application No. 09/614,092 or were cited by the Examiner during prosecution of the parent application. Pursuant to 37 C.F.R. §1.98(d), applicants have not enclosed copies of the

listed documents herewith. However, applicants stand ready to provide copies at the Examiner's request.

Applicants respectfully request that the above documents be (1) fully considered by the Examiner during the course of the examination of this application and (2) printed on any patent issuing from this application. Applicants also request that a copy of the enclosed Form PTO-1449 duly initialed by the Examiner be forwarded to the undersigned with the next communication.

Respectfully submitted,

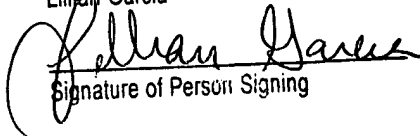


Jane T. Gunnison (Reg. No. 38,479)
Attorney for Applicants
R. Minako Pazdera (Reg. No. 46,984)
Agent for Applicants
c/o FISH & NEAVE
Customer No. 1473
1251 Avenue of the America
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax.: (212) 596-9090

I hereby certify that this
Correspondence is being
deposited with the U.S.
Postal Service as First
Class Mail in an envelope
Addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450 on

November 24, 2003

Lillian Garcia


Signature of Person Signing

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.17 CONAPPLICATION NO.
10/658,521INFORMATION DISCLOSURE
STATEMENT BY APPLICANTAPPLICANT
R. Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 8, 2003GROUP
Not yet assigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,950,599	08/21/90	Bertling	435	172.3	
	4,959,313	09/25/90	Taketo	435	69.1	
	5,204,244	04/20/93	Fell et al.	435	69.6	
	5,286,647	02/15/94	Handley et al.	435	344	
	5,545,806	08/13/96	Lonberg et al.	800	2	
	5,545,807	08/13/96	Surani et al.	800	2	
	5,569,825	10/29/96	Lonberg et al.	800	2	

FOREIGN PATENT DOCUMENTS

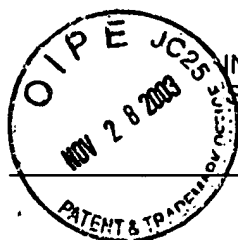
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	EP 0 298 807 A1	01/11/89	Europe				
	EP 0 315 062 B1	05/10/89	Europe				
	EP 0 322 240 B1	06/28/89	Europe				
	EP 0 459 372 A3	12/04/91	Europe				
	EP 0 463 151 B1	01/02/92	Europe				
	WO 90/04036	04/19/90	PCT				
	WO 91/00906	01/24/91	PCT				
	WO 91/10741	07/21/91	PCT				
	WO 92/03918	03/19/92	PCT				
	WO 92/22645	12/23/92	PCT				
	WO 93/05165	03/18/93	PCT				
	WO 93/12227	06/24/93	PCT				
	WO 94/00569	01/06/94	PCT				
	WO 94/02602	02/03/94	PCT				
	WO 94/25585	11/10/94	PCT				
	WO 96/34096	10/31/96	PCT				

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.17 CONAPPLICATION NO.
10/658,521INFORMATION DISCLOSURE
STATEMENT BY APPLICANTAPPLICANT
R. Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 8, 2003GROUP
Not yet assigned

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

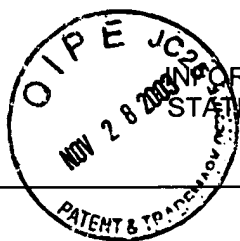
EXAMINER INITIAL	
	Albertsen et al., "Construction and characterization of a yeast artificial chromosome library containing seven haploid human genome equivalents," <i>Proc. Natl. Acad. Sci.</i> 87:4256-4260 (1990)
	Aldhous, "Transgenic mice display a class (switching) act," <i>Science</i> 262:1212-
	Ayares, et al., "Sequence homology requirements for intermolecular recombination in mammalian cells," <i>Proc. Natl. Acad. Sci.</i> 83:5199-5203 (1986)
	Berman, et al., "Content and organization of the human Ig V _H locus: definition of three new V _H families and linkage to the Ig C _H locus, <i>EMBO J.</i> 7:727-738 (1988)
	Blankenstein et al., "Immunoglobulin VH region genes of the mouse are organized in overlapping clusters," <i>Eur. J. Immunol.</i> 17:1351-1357 (1987)
	Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice," <i>Proc. Natl. Acad. Sci.</i> 85:836-840 (1988)
	Brownstein et al., "Isolation of single-copy human genes from a library of yeast artificial chromosome clones," <i>Science</i> 244:1348-1351 (1989)
	Brüggemann et al., "A repertoire of monoclonal antibodies with human heavy chains from transgenic mice," <i>Proc. Natl. Acad. Sci.</i> 86:6709-6713 (1989)
	Brüggemann et al., "Construction, function and immunogenicity of recombinant monoclonal antibodies," <i>Behring Inst. Mitt.</i> 87:21-24 (1990)
	Brüggemann et al., "Human antibody production in transgenic mice: expression from 100 Kb of the human IgH locus," <i>Eur. J. Immunol.</i> 21:1323-1326 (1991)
	Burke et al., "Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors," <i>Science</i> 236:806-812 (1987)
	Buttin, et al., "Exogenous Ig gene rearrangement in transgenic mice: a new strategy for human monoclonal antibody production," <i>Trends in Genetics</i> 3(8):205-206 (1987)
	Cai, J. et al., "Extensive and selective mutation of a rearranged V _H 5 gene in human B cell chronic lymphocytic leukemia," <i>J. Exp. Med.</i> 176:1073-1081 (1992)
	Capecchi, et al., "Altering the genome by homologous recombination," <i>Science</i> 244:1288-1292 (1989)
	Chen et al., "Immunoglobulin gene rearrangement in B cell deficient mice generated by targeted deletion of the J _H locus," <i>International Immunology</i> 5:647-656 (1993)
	Choi, et al., "RNA splicing generates a variant light chain from an aberrantly rearranged κ gene," <i>Nature</i> 286:776-779 (1980)
	Choi, et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome," <i>Nature Genetics</i> 4:117-123 (1993)
	Cook, G.P. et al. "The human immunoglobulin V _H repertoire," <i>Immunology Today</i> 16:237-242 (1995)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.17 CONAPPLICATION NO.
10/658,521APPLICANT
R. Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 8, 2003GROUP
Not yet assignedINFORMATION DISCLOSURE
STATEMENT BY APPLICANT

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

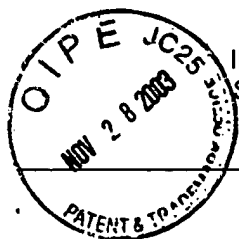
EXAMINER INITIAL	
	Corvalon, et al., "Generation of fully human high affinity monoclonal antibodies to EGF receptor in mice," <i>Journal of Allergy and Clinical Immunology</i> 99:S214 (1997)
	Cox Declaration, from United States Patent No. 5,545,806.
	Davies et al., "Targeted alterations in yeast artificial chromosomes for inter-species gene transfer," <i>Nucleic Acids Res.</i> 20:2693-2698 (1992)
	Doetschman, et al., "Targeted mutation of the <i>hprt</i> gene in mouse embryonic stem cells," <i>Proc. Natl. Acad. Sci.</i> 85:8583-8587 (1988)
	Dorfman, N.A., "The optimal technological approach to the development of human hybridomas," <i>J. Biol. Resp. Modif.</i> 4:213-239 (1985)
	Eliceiri et al., "Stable integration and expression in mouse cells of yeast artificial chromosomes harboring human genes," <i>Proc. Natl. Acad. Sci.</i> 88:2179-2183 (1991)
	Ellison et al., "The nucleotide sequence of a human immunoglobulin C _γ 1 gene," <i>Nucleic Acids Research</i> 10:4071-4079 (1982)
	Emery, S.C. et al., "Humanised monoclonal antibodies for therapeutic applications," <i>Expert Opinion on Investigation Drugs</i> 3:241-251 (1994)
	Fishwild et al., "High-avidity human IgG _k monoclonal antibodies from a novel strain of minilocus transgenic mice," <i>Nature Biotech.</i> 14:845-851 (1996)
	Garza et al., "Mapping the <i>drosophila</i> genome with yeast artificial chromosomes," <i>Science</i> 246:641-646 (1989)
	Gnirke et al., "Cloning and in vivo expression of the human GART gene using yeast artificial chromosomes," <i>EMBO J.</i> 10(7):1629-1634 (1991)
	Green, et al., "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACs," <i>Nature Genetics</i> 7:13-21 (1994)
	Huber, et al., "The human immunoglobulin κ locus. Characterization of the partially duplicated L regions," <i>Eur. J. Immunol.</i> 23:2860-2967 (1993)
	Huxley et al., "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion," <i>Genomics</i> 9:742-750 (1991)
	Ikematsu, et al., "Clonal analysis of a human antibody response. II. sequences of the V _H genes of human IgM, IgG, IgA to rabies virus reveal preferential utilization of V _H III segments and somatic hypermutation," <i>The Journal of Immunology</i> 150:1325-1337 (1993)
	Jakobovits, et al., "Analysis of homozygous mutant chimeric mice: Deletion of the immunoglobulin heavy-chain joining region blocks B-cell development and antibody production," <i>Proc. Natl. Acad. Sci.</i> 90:2551-2555 (1993)
	Jakobovits, et al., "Germ-line transmission and expression of a human-derived yeast artificial chromosome," <i>Nature</i> 362:255-258 (1993)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.17 CONAPPLICATION NO.
10/658,521INFORMATION DISCLOSURE
STATEMENT BY APPLICANTAPPLICANT
R. Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 8, 2003GROUP
Not yet assigned

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

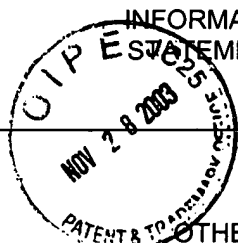
EXAMINER INITIAL	
	Jakobovits, "Humanizing the mouse genome," <i>Current Biology</i> 4:761-763 (1994)
	Jakobovits, et al. "Production of antigen-specific human antibodies from mice engineered with human heavy and light chain YACs," <i>Annals of the New York Academy of Sciences</i> 764:525-535 (1995)
	Jakobovits, A., "Production of fully human antibodies by transgenic mice," <i>Current Opinion in Biotechnology</i> 6:561-566 (1995)
	Jakobovits et al., "Humoral immunity in mice engineered with megabase human heavy and kappa light chain YACs," <i>Journal of Allergy and Clinical Immunology</i> , 99:S113 (1997)
	Johnson, et al., "Targeting of nonexpressed genes in embryonic stem cells via homologous recombination," <i>Science</i> 245:1234-1236 (1989)
	Joyner et al., "Production of a mutation in mouse En-2 gene by homologous recombination in embryonic stem cells," <i>Nature</i> 338:153-155 (1989)
	Koller et al., "Inactivating the β_2 -microglobulin Locus in Mouse Embryonic Stem Cells by Homologous Recombination," <i>Proc. Natl. Acad. Sci.</i> 86:8932-8935 (1989)
	Kucherlapati, R., "Homologous Recombination in Mammalian Somatic Cells," <i>Prog. Nucleic Acid Res. Mol. Biol.</i> 36:301-310 (1989)
	Li Y. et al., "The binding specificity of human V _H 4-34 (V _H 4-21) encoded antibodies is determined by both V _H framework region 1 and complementarity determining region 3," <i>J. Mol. Biol.</i> 256:577-589 (1996)
	Lonberg et al., "Antigen-specific human antibodies from mice comprising four distinct genetic modifications," <i>Nature</i> 368:856-859 (1994)
	Lonberg, et al., "Human antibodies from transgenic mice," <i>International Reviews of Immunology</i> 13:65-93 (1995)
	Mansour, et al., "Disruption of the proto-oncogene <i>Int-2</i> In mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes," <i>Nature</i> 336:348-352 (1988)
	Matsuda et al., "Structure and physical map of 64 variable segments in the 3' 0.8-megabase region of the human immunoglobulin heavy-chain locus," <i>Nature Genet.</i> 3:88-94 (1993)
	Max, et al., "Sequences of five potential recombination sites encoded close to an immunoglobulin κ constant region gene," <i>Proc. Natl. Acad. Sci.</i> 76(7):3450-3454 (1979)
	Mendez, et al., "Analysis of the structural integrity of YACs comprising human immunoglobulin genes in yeast and in embryonic stem cells," <i>Genomics</i> , 26:294-307 (1995)
	Mendez, et al., "Functional transplant of megabase human immunoglobulin loci recapitulates human antibody response in mice," <i>Nature Genetics</i> 15:146-156 (1997)
	Miller, et al., "Structural alterations in J regions of mouse immunoglobulin λ genes are associated with differential gene expression," <i>Nature</i> 295:428-430 (1982)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.17 CON	APPLICATION NO. 10/658,521
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT R. Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 8, 2003	GROUP Not yet assigned



OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

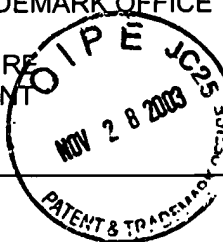
EXAMINER INITIAL	
	Morrison, "Success in specification," <i>Nature</i> 368:812-813 (1994)
	Mortensen et al., "Production of homozygous mutant ES cells with a single targeting construct," <i>Mol. Cell. Biol.</i> 12(5):2391-2395 (1992)
	Orkin, et al., "Mutation in an intervening sequence splice junction in man," <i>Proc. Natl. Acad. Sci.</i> 78(8):5041-5045 (1981)
	Pachnis et al., "Transfer of a yeast artificial chromosome carrying human DNA from <i>saccharomyces cerevisiae</i> into mammalian cells," <i>Proc. Natl. Acad. Sci.</i> 87:5109-5113 (1990)
	Pavan et al., "Modification and transfer into an embryonal carcinoma cell line of a 360-kilobase human-derived yeast artificial chromosome," <i>Mol. Cell. Biol.</i> 10(8):4163-4169 (1990)
	Rajewsky, et al., "Evolutionary and somatic selection of the antibody repertoire in the mouse," <i>Science</i> 238:1088-1094 (1987)
	Ramirez-Solis, et al., "Chromosome engineering in mice," <i>Nature</i> 378:720-724 (1995)
	Sakano, et al., "Sequences at the somatic recombination sites of immunoglobulin light-chain genes," <i>Nature</i> 280:288-294 (1979)
	Sakano, et al., "Two types of somatic recombination are necessary for the generation of complete immunoglobulin heavy-chain genes," <i>Nature</i> 286:676-683 (1980)
	Sanz, I., "Multiple mechanisms participate in the generation of diversity of human H chain CDR3 regions," <i>J. of Immunol.</i> 147:1720-1729 (1991)
	Schedl, et al., "Transgenic mice generated by pronuclear injection of a yeast artificial chromosome," <i>Nucl. Acids Res.</i> 20:3073-3077 (1992)
	Schedl, et al., "A method for the generation of YAC transgenic mice by pronuclear microinjection," <i>Nucleic Acids Research</i> 21(20):4783-4787 (1993)
	Schedl, et al., "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice," <i>Nature</i> 362:258-261 (1993)
	Schwartzberg et al., "Germ-line transmission of a <i>c-abl</i> mutation produced by targeted gene disruption in ES cells," <i>Science</i> 246:799-803 (1989)
	Seidman, et al., "A Mutant Immunoglobulin light Chain is Formed by Aberrant DNA- and RNA-Splicing Events," <i>Nature</i> 286:779-783 (1980)
	Shimizu, et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse," <i>Proc. Natl. Acad. Sci.</i> 86:8020-8023 (1989)
	Shin et al., "Physical map of the 3' region of the human immunoglobulin heavy chain locus: clustering of autoantibody-related variable segments in one haplotype," <i>EMBO J.</i> 10:3641-3645 (1991)
	Straus, et al., "Germ line transmission of a yeast artificial chromosome spanning the murine $\alpha_1(1)$ collagen locus," <i>Science</i> 259:1904-1907 (1993)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.17 CON	APPLICATION NO. 10/658,521
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT R. Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 8, 2003	GROUP Not yet assigned



OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

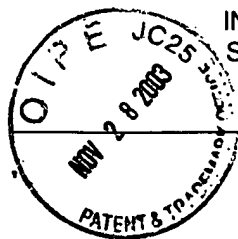
EXAMINER INITIAL	
	Taggart et al., "Stable antibody-producing murine hybridomas," <i>Science</i> 219:1228-1230 (1983)
	Taki, et al., "Targeted insertion of a variable region gene into the immunoglobulin heavy chain locus," <i>Science</i> 262:1268-1271 (1993)
	Taylor, et al., "Human immunoglobulin transgenes undergo rearrangement, somatic mutation and class switching in mice that lack endogenous IgM," <i>International Immunol.</i> 6:579-591 (1994)
	Taylor, et al., "A transgenic mouse that expresses a diversity of human sequence heavy and light chain immunoglobulins," <i>Nucleic Acids Research</i> 20:6287-6295 (1992)
	Thomas et al., "Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells," <i>Cell</i> 51:503-512 (1987)
	Traver, et al., "Rapid screening of a human genomic library in yeast artificial chromosomes for single-copy sequences," <i>Proc. Natl. Acad. Sci.</i> 86:5898-5902 (1989)
	Treisman, et al., "Specific transcription and RNA splicing defects in five cloned β -thalassaemia genes," <i>Nature</i> 302:591-596 (1983)
	Tuaillon, et al., "Analysis of direct and inverted DJ _H rearrangements in a human Ig heavy chain transgenic minilocus," <i>J. Immunol.</i> 154:6453-6465 (1995)
	Tuaillon, et al., "Human immunoglobulin heavy-chain minilocus recombination in transgenic mice: gene-segment use in μ and γ transcripts," <i>Proc. Natl. Acad. Sci.</i> 90:3720-3724 (1993)
	Tucker et al., "Mouse IgA heavy chain gene sequence: implications for evolution of immunoglobulin hinge exons," <i>Proc. Natl. Acad. Sci.</i> 78:7684-7688 (1981)
	Wagner, et al., "The diversity of antigen-specific monoclonal antibodies from transgenic mice bearing human immunoglobulin gene miniloci," <i>Eur. J. Immunol.</i> 24:2672-2681 (1994)
	Weichhold, et al., "The human immunoglobulin κ locus consists of two copies that are organized in opposite polarity," <i>Genomics</i> 16:503-511 (1993)
	Winter, et al., "Making antibodies by phage display technology," <i>Annual Review of Immunology</i> 12:433-455 (1994)
	Yamada, M., et al., "Preferential utilization of specific immunoglobulin heavy chain diversity and joining segments in adult human peripheral blood B lymphocytes," <i>J. Exp. Med.</i> 173:395-407 (1991)
	Yamamura, et al., "Cell-type-specific and regulated expression of a human γ 1 heavy-chain immunoglobulin gene in transgenic mice," <i>Proc. natl. Acad. Sci.</i> 83:2152-2156 (1986)
	Yancoupoulos, et al. "Developmentally controlled and tissue-specific expression of unrearranged V _H gene segments," <i>Cell</i> 40:271-281 (1985)
	Yancoupoulos, et al., "Reconstruction of an immune system," <i>Science</i> 241:1581-1583 (1988)
	Yang, et al., "Human monoclonal antibodies to human TNF-alpha generated from mice carrying human Ig loci," <i>Journal of Allergy and Clinical Immunology</i> 99:S15 (1997)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.17 CONAPPLICATION NO.
10/658,521APPLICANT
R. Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 8, 2003GROUP
Not yet assignedINFORMATION DISCLOSURE
STATEMENT BY APPLICANT

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Zachau., "The Human immunoglobulin κ locus and some of its acrobatics," <i>Biol. Chem.</i> 371:1-6 (1990)
	Zijlstra, et al., "Germ-line transmission of a disrupted β_2 -microglobulin gene produced by homologous recombination in embryonic stem cells, <i>Nature</i> 342:435-438 (1989)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.